

EDITORIAL COMMENT

Dilate or Defer? View of a Skeptic*

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Coronary angioplasty was developed by Andreas Gruentzig as a less invasive method to alleviate ischemia and the debilitating angina it causes. The introduction of balloon dilation and the subsequent improvements, especially stenting, is a resounding success story in medicine. Bypass surgery has been safely avoided as demonstrated in many randomized trials. Although subsets of patients with extensive disease, especially those with diabetes, have fared better with surgery, angioplasty and stenting have far surpassed surgery as the most frequently performed revascularization procedures.

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Many patients with coronary artery disease do not have debilitating symptoms, and the data to support revascularization in these have undergone less scrutiny. The absence of severe symptoms does not assure a good prognosis, and the extent of coronary artery disease, the magnitude of ischemia, and left ventricular function define patients who have an improved prognosis with surgery and probably (by inference) percutaneous intervention. There are, however, many patients without refractory symptoms who lack the prognostic indicators mandating revascularization. Many of these are undergoing percutaneous interventions all over the world and, yet, evidence for the true value of that approach has been sparse.

The Randomized Treatment of Angina (RITA)-2 trial was designed to compare the strategy of performing percutaneous transluminal coronary angioplasty (PTCA) or medical therapy alone on patients who were judged eligible for either approach. The primary end point was death or myocardial infarction (MI) at five years. In this issue of the *Journal*, Henderson et al. (1) report the results: the primary end point, death or MI, was not different, and death alone was not different (43 in each group). The need for subsequent bypass surgery was not different. Repeat percutaneous intervention was more in the patients who did not receive it in the first place, but that difference was not great, 17% of the medical group and 27% in the PTCA group at five years. Subsequent revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]) was used in 23.3% of the PTCA and 28.8% of the surgery

patients. As reported by Henderson et al. (1), angina was improved, especially during the first year; however, that difference narrowed over time due to the performance of PCI in symptomatic patients in the medical group. Why was the outcome so disappointing for PTCA? Many will dismiss this study as dated. "It is so 90s." This may be true. Let this skeptic examine the evidence.

The skeptic: "This is a low-risk group." The overall mortality at five years of 4.6% in the PTCA group and 4.7% in the medical group would not argue for an abundance of high-risk features. Sixty percent of the patients had single-vessel disease at baseline. The National Heart, Lung, and Blood Institute Dynamic registry of PCI in high volume centers was composed of one-vessel disease (40.6%), two-vessel disease (32.3%), and three-vessel (26.8%), and a single lesion was treated in 68.2% of these cases (2). So, are the lesions treated in this study markedly different from those in elective patients, without the exclusions listed in this trial, who are undergoing PCI today? I suspect not.

The skeptic: "This is old technology, results would be much better today." Stenting was used in this trial only to bail out complications of PTCA. Emergency surgery was used in 1.5% (7 of 471), which is not an unusually high number even in the stent era. In the NHLBI Dynamic registry, it has been 1.1% (2).

The skeptic: "Surely stenting has a better outcome than plain old balloon angioplasty." The findings of a recent meta-analysis of 29 trials of routine stenting versus balloon angioplasty and stenting only for complications or residual stenosis may be surprising. Death, death or MI, and subsequent coronary bypass surgery were not different (3). Repeat PCI was more common in the balloon angioplasty with provisional stenting group, but the absolute difference was only 5 patients per 100 treated. Stenting was used more commonly in the control group in these trials, but the almost identical death, MI, and CABG rates by treatment group are reminiscent of the present study. Routine stenting may have changed the primary outcome of this trial, but the evidence to assume that is lacking.

The skeptic: "English patients will put up with anything." American colleagues may feel that the subjects of this trial will keep the proverbial "stiff upper lip" and que passively for staggering doses of anti-anginal medications to combat their angina. (English colleagues in turn may feel that Americans have the "princess and the pea" syndrome and will be dilated at the slightest twinge or any hint of ischemia). Medical systems are different, but the consumption of antianginals was not dramatically different between these treatment groups. At all time points there was more angina in the medical group, and this may have been reduced by more aggressive interventions. However, the absence of more interventions in the medical group did not seem to adversely affect the primary end point of death or MI.

The skeptic: "It is true that the use of beta-blockers, angiotensin-converting enzyme inhibitors, lipid-lowering

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agents, and thianopyridines seem very low by current standards." These agents exert their beneficial effect primarily over the extended follow-up and would be expected to benefit the medical group as well as the PTCA group. Only glycoprotein IIb/IIIa agents have been shown to reduce periprocedural MI significantly. Routine biomarkers were not obtained in this study, but the occurrence of periprocedural MI, although small, did not translate into an increase in late events.

The skeptic: "Let's get back to the angina. At the end of the follow-up, grade II or more angina was present in 21.4% of the medical patients but only 15.0% of the PTCA group. ($\Delta 6.4\%$; 95% confidence interval, 1.5 to 11.3; $p = 0.011$). That is about a 30% reduction in angina." Of course, for patients with a less stiff upper lip, an intervention could be done.

The skeptic: "At least they could exercise more." Yes, 25 s more at 3 years!

This skeptic is beginning to run out of ammunition. Maybe the Clinical Outcome Utilizing Revascularization and Aggressive drug Evaluation (COURAGE) trial and the Bypass Angioplasty Revascularization Investigation-2 Diabetes (BARI 2D) will come to my rescue at least in some subsets, like diabetes (only 9% of the patients in this trial had treated diabetes).

What can we learn from this trial that can be applied to the next patient we see? As the authors point out, if there is no evident prognostic marker that the patient is at increased risk, then use revascularization to solve refractory symptoms. This will vary among patients. Some will have a strong desire to avoid angina so as to engage in vigorous activities.

Others will be intolerant of beta-blockers. We must, however, be honest with ourselves as well as our patients. If prognosis is not an issue, that should be clearly stated. Physicians have been accused of having the "oculostenotic reflex." Patients who are told that they have a "blockage" often have an "auditorystenotic reflex." "If it is blocked, I want it fixed." If there is no evidence to support improvement in prognosis, the patient needs to hear and understand that. Then, if the symptoms warrant an intervention, the patient can help make the decision.

In the coming era of drug-eluting stents, the cost to the medical system will increase. Physicians must evaluate this advance for its contribution to preventing the hard end points of death and MI. Industry and payors must provide a balance in pricing and reimbursement for all patients who require revascularization. Cost containment can be achieved by avoiding intervention in those who do not. RITA-2 supports what we all should know and practice.

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